Balo disease, HIV- or HTLV-myelopathy, progressive multifocal leucoencephalopathy, or a secondary demyelinating disorder.

36. The pharmaceutical composition of claim 35, wherein the secondary demyelinating disorder is CNS lupus erythematodes, polyarteriitis nodosa, Sjögren syndrome, sarcoidosis or isolated cerebral vasulitis.

37. A pharmaceutical composition for treating a demyelinating disorder comprising an inhibitor of the interaction of glutamate with the α-amino-3-hydroxy-5-methyl-4-isoxazole-propionate (AMPA) receptor complex and a pharmaceutically acceptable carrier, wherein the inhibitor is the AMPA receptor channel blocker fluorowillardiine.

38. A pharmaceutical composition for treating a demyelinating disorder comprising an inhibitor of the interaction of glutamate with the α-amino-3-hydroxy-5-methyl-4-isoxazole-propionate (AMPA) receptor complex and a pharmaceutically acceptable carrier, wherein the inhibitor is combined with one or more of: an immunosuppresive agent (e.g. corticotrophin, a glucocorticoid, cyclophosphamide, cyclosporine, azothioprine or mitozantrone), an interferon (IFN; IFN-beta-1a e.g. Rebif and Avonex; IFN-beta-lb e.g. Betaseron and Betaferon; IFN-alpha-2a e.g. Alphaferone; IFN-alpha-2b e.g. Viraferon), a phosphodiesterase type IV inhibitor, a humanised monoclonal antibody against a leukocyte adhesion molecule (e.g. Antegran), a synthetic polypeptide (e.g. glatiramer acetate, copolymer-1), a tissue matrix metalloproteinase (MMP) inhibitor (e.g. hydroxamic acid-based inhibitors of MMPs), or a tumour necrosis factor (TNF) inhibitor (e.g. Thalidomide or TNF-receptor immunoglobulin fusion protein).

REMARKS

In the Office Action dated July 29, 2002, the Examiner made final the Restriction Requirement of March 19, 2002, recognized Applicants' election with traverse of the claims of Group I (claims 1, 2, 4-6, 8-10, 12, 14, and 18-20), and withdrew from consideration the non-elected claims of Group II (claims 3, 7, 11, and 13). Applicants

reserve the right to file one or more divisional applications claiming the non-elected subject matter.

Upon entry of the present Amendment, claims 21-38 are pending in the application. Claims 1-14 and 18-20 have been canceled.

In the amendment submitted herewith, new claims 21-38 have been added. New claims 21-38 more clearly define the subject matter that Applicants regard as their invention. Applicants submit that the new claims are consistent with the elected subject matter of Group I. No new matter has been added by this amendment, as support for the new claims is found throughout the specification and in the original claims. Entry of this amendment is respectfully requested.

Each of the objections and rejections presented in the Office Action of July 29, 2002 is addressed individually below.

Rejection of claims 1, 2, 4-6, 8, and 9 under 35 U.S.C. § 102(e)

Claims 1, 2, 4-6, 8, and 9 were rejected under 35 U.S.C. § 102(e) as anticipated by Csuzdi et al., U.S. Patent No. 6,323,187 ("Csuzdi et al.").

Applicants respectfully traverse this rejection. Csuzdi et al. is not § 102(e) prior art to the present application. The Examiner indicated that the filing date of Csuzdi et al. is July 31, 1998, which is the § 102(e) date listed on the face of the patent. The Examiner also recognized Applicants' claim for foreign priority to GB9814380, filed July 2, 1998. Since Applicants' foreign priority date of July 2, 1998 pre-dates the § 102(e) date of Csuzdi et al. of July 31, 1998, Csuzdi et al. does not constitute § 102(e) prior art to the present application. Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection under § 102(e).

However, Applicants present the following arguments in the event that the Examiner would cite the corresponding Csuzdi et al. PCT publication WO97/28163, published on August 7, 1997, as § 102(a) prior art.

Applicants' invention as presently claimed relates to pharmaceutical compositions and methods for treating demyelinating disorders using inhibitors of the interaction of glutamate with the AMPA receptor complex. The Examiner asserted that

Csuzdi et al. teach condensed 2,3-benzodiazepine derivatives, including amino- or desamino-2,3-benzodiazepine, compositions comprising such compounds, and their use as AMPA receptor inhibitors. However, the disclosure of Csuzdi et al. relating to neurological and psychiatric disorders that are triggered by over-stimulation of the AMPA receptor (col. 4, lines 8-27) refers only to disorders that are neurodegenerative disorders, and are not demyelinating disorders. Therefore, the disclosure of Csuzdi et al. is not relevant to Applicants' invention as it relates to the treatment of demyelinating disorders.

Furthermore, the rejected claims 1, 2, 4-6, 8, and 9 have been canceled, and Applicants' new pharmaceutical composition claims 31-37 do not recite amino- or desamino-2,3-benzodiazepine, the species asserted by the Examiner as being disclosed by Csuzdi et al. The particular 2,3-benzodiazepine derivatives recited in new pharmaceutical composition claim 34, namely, 1-(4-aminophenyl)-4-methyl-7,8-methylene-dioxy-5H-2,3-benzodiazepine (GYKI52466) and (-)1-(4-aminophenyl)-4-methyl-7,8-methylenedioxy-4,5-dihydro-3-methylcarbamoyl-2,3-benzodiazepine (GYK153773), are not disclosed by Csuzdi et al. Accordingly, Applicants submit that the new claims submitted herewith are novel and non-obvious over Csuzdi et al.

Rejection of claims 1, 2, 4, 5, 10, and 12 under 35 U.S.C. § 102(b)

Claims 1, 2, 4, 5, 10, and 12 were rejected under 35 U.S.C. § 102(b) as being anticipated by Keller et al., DE 4239816 A1 ("Keller et al."). The Examiner stated that Keller et al. disclose an AMPA receptor channel blocker, Joro spider toxin, and a composition comprising this molecule.

Applicants respectfully traverse this rejection. As discussed above, Applicants' claimed invention relates to pharmaceutical compositions and methods for treating demyelinating disorders using inhibitors of the interaction of glutamate with the AMPA receptor complex. Keller et al. disclose the use of toxins, including Joro spider toxin, for inhibiting glutamate-induced synaptic stimulus transfer in the central nervous system of mammals. However, the central nervous system diseases referred to by Keller et al., including Alzheimer's Disease, Parkinson's Disease, and types of epilepsy (see page 2,

lines 6-15), are neurodegenerative disorders, and are not demyelinating disorders. Therefore, the disclosure of Keller et al. is not relevant to Applicants' invention as it relates to the treatment of demyelinating disorders.

Moreover, the rejected claims 1, 2, 4, 5, 10, and 12 have been canceled, and Applicants' new pharmaceutical composition claims 31-37 do not encompass Joro spider toxin. Therefore, Applicants respectfully submit that this rejection under § 102(b) has been overcome and should be reconsidered and withdrawn.

Objection to claims 1, 2, 4, 5, 8, 14, and 18-20

Claims 1, 18, and 19 were objected to as reciting the abbreviation "AMPA" without spelling out the full term being abbreviated. Claims 1, 18, and 19 have been canceled, and all of the new independent claims (claims 21, 29, 31, 34, 37, and 38) spell out the full term for AMPA. Accordingly, this objection has been overcome and should be withdrawn.

The Examiner noted that there were two periods at the end of claim 2. Claim 2 has been canceled, rendering this objection moot.

The Examiner also noted typographical errors in claims 8 and 9. Claims 8 and 9 have been canceled, rendering this objection moot.

Claims 1, 4, 5, 14, and 18-20 were objected to as reciting non-elected subject matter, namely, an inhibitor of the interaction of glutamate with the kainite receptor. Claims 1, 4, 5, 14, and 18-20 have been canceled, and new claims 21-38 do not refer to inhibitors of the interaction of glutamate with the kainite receptor. Accordingly, Applicants respectfully submit that this objection has been overcome and should be withdrawn.

Information Disclosure Statement

In the Office Action dated July 29, 2002, the Examiner indicated that a PTO-1449 form and copies of the references cited were not received in conjunction with the Information Disclosure Statement filed on May 7, 2001. Accordingly, Applicants submit

herewith copies of the PTO-1449 form and cited references as originally submitted on May 3, 2001.

A Supplemental Information Disclosure Statement is also submitted herewith. This Information Disclosure Statement is submitted pursuant to 37 C.F.R. § 1.56 and is filed in accordance with 37 C.F.R. § 1.97(c) before the mailing date of a final action, notice of allowance, or action closing prosecution. As the Information Disclosure Statement is being filed after the mailing date of a first Office Action on the merits, the Commissioner is hereby authorized to deduct the $180.00 submission fee from our Deposit Account No. 08-0219.

Applicants respectfully request that the disclosed references be expressly considered during the prosecution of this application and that the references be made of record therein and appear among the "References Cited" on any patent to issue therefrom.

This submission does not constitute a representation by Applicants that an exhaustive search has been conducted or that no other relevant information exists, and does not constitute an admission that any of the listed documents are material or constitute "prior art." Moreover, Applicants understand that the Examiner will make an independent evaluation of the cited references. Applicants reserve the right to take appropriate action to establish the patentability of the disclosed invention over the listed documents, should one or more of them be applied against the claims of the present application.

Copies of the documents listed on the attached Form PTO-1449, along with a copy of a third party submission to the European Patent Office in a related European patent application, are submitted herewith. It is respectfully requested that the Examiner initial and return a copy of both of the enclosed PTO-1449 forms (original and supplemental) with the next Patent Office communication.

Conclusion

For the reasons set forth above, Applicants contend that all of the objections and rejections in the Office Action dated July 29, 2002 have been overcome and should be

reconsidered and withdrawn. Applicants respectfully submit that the claims are in condition for allowance.

Applicants hereby petition for a two-month extension of time pursuant to 37 C.F.R. § 1.136 to respond to the Office Action mailed on July 29, 2002. Please deduct the $400.00 fee for this purpose from our Deposit Account No. 08-0219. Please charge any other payments due or credit any overpayments to our Deposit Account No. 08-0219.

Respectfully submitted,

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Dated: Dec. 27, 2002

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